

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/005936

International filing date (day/month/year)
02.06.2004

Priority date (day/month/year)
02.06.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/74

Applicant
B.R.A.I.N. BIOTECHNOLOGY RESEARCH AND ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/005936

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/005936

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-21
	No: Claims	
Inventive step (IS)	Yes: Claims	11-12
	No: Claims	1-10, 13-21
Industrial applicability (IA)	Yes: Claims	1-21
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item V.

- 1 The following documents are referred to in this communication:

D2 : STEDMAN KENNETH M ET AL: "Genetic requirements for the function of the archaeal virus SSV1 in *Sulfolobus solfataricus*: Construction and testing of viral shuttle vectors" GENETICS, vol. 152, no. 4, August 1999 (1999-08), pages 1397-1405, XP002292796 ISSN: 0016-6731

D3 : STEDMAN K, ZILLIG W, SCHLEPER C, MARTUSEWITSCH W, VAN DER OOST J: "Extremophile Genetics" SECOND ASTROBIOLOGY SCIENCE CONFERENCE, 7 April 2002 (2002-04-07), XP002292797 INTERNET

D4: STEDMAN KENNETH M ET AL: "Relationships between fuselloviruses infecting the extremely thermophilic archaeon *Sulfolobus*: SSV1 and SSV2." RESEARCH IN MICROBIOLOGY, vol. 154, no. 4, May 2003 (2003-05), pages 295-302, XP002292798 ISSN: 0923-2508

- 2 Document D2 discloses a fully functional viral shuttle vector for *S.solfataricus* and *E.coli*. The vector is based on the SSV1 virus. The document discusses the importance of the viral integrase gene and the use of the Tind promoter for regulated expression or over expression of genes in *S.solfataricus*. The document teaches that "Expression and complementation studies using this shuttle vector are underway".

Document D3 discloses the fact that a shuttle vector was developed based on SSV1 sequences. With this vector a heterologous gene expression in *S.solfataricus* was performed. The document discloses that it is possible, by using an expression vector, to express a heterologous protein in *S.solfataricus*.

Document D4 discloses a comparison of SSV1 and SSV2 fuselloviruses. It shows that the integrase genes of both viruses are conserved. It further states that both viruses are obviously homologues.

2.1 INDEPENDENT CLAIM 1

- 2.1.1 Document D2, which is considered to represent the most relevant state of the art, discloses a vector from which the subject-matter of independent claim 1 differs in that the vector of the application should contain a selectable

marker gene and a *Sulfolobus* promoter.

- 2.1.2 The problem to be solved by the present invention may therefore be regarded as the provision of a further expression vector system for *Sulfolobus* wherein said system comprises a selectable marker and a *Sulfolobus* promoter.
- 2.1.3 In view of D3 the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: D3 already discusses successful gene transfer using SSV1 based vectors. The skilled person was therefore well aware of the fact that such vectors do exist and work properly. In a further aspect, the features of the vector listed in claims 1(a), (c) and (d) are common features every expression vector has when it is to be used in *Sulfolobus*. The features of (b) are already known from D2. It is furthermore not derivable from the application that such a broadly claimed vector indeed offers a beneficial effect over the vectors already disclosed in the art. The application does not provide for any comparative tests that allow the justification that the vector of claim 1 offers any additional technical effect over the vector disclosed in D2. The restriction to the SSV1 homologues SSV2/pSSVX is also obvious as the skilled person would take the teaching of D4 into account.
- 2.1.4 Therefore the features disclosed in D2, D3 and D4 would be combined by the skilled person, without exercise of any inventive skills in order to solve the problem posed. The proposed solution in independent claim 1 thus cannot be considered inventive (Article 33(3) PCT).
- 2.2 Independent claim 13 is directed to a shuttle vector. However, shuttle vectors as such are already known from D2. The subject matter of claim 13 is only a further variation that is obvious for the skilled person, consequently claim 13 does not fulfil the requirements of Art.(33(3) PCT). The same argumentation applies mutatis mutandis to the subject matter of independent claims 15 and 18-21.
- 3 **DEPENDENT CLAIMS 2-10, 14, 16, 17**
Dependent claims 2-10, 14, 16, 17 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).

4 DEPENDENT CLAIMS 11, 12

The combination of the features of dependent claims 11, 12 are neither known from, nor rendered obvious by, the available prior art. The reasons are as follows:

The claims relate to the use of specific promoter sequences and reporter proteins that are neither taught nor suggested to be used in an expression vector as claimed in claim 1. The use of said sequences in combination with the expression vector of claim therefore fulfills the requirements of Art.33(3) PCT.